Benefits and Risks of OPV Use

Olen Kew, Ph.D.
Division of Viral Diseases
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention

Polio Immunization: Moving Forward

NIAID/NIH Bethesda

19–20 September 2007

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

OPV: Advantages

- Main tool for global polio eradication
- Confers mucosal (intestinal) immunity
- Suitable for mass campaigns
  - Synchronous immunity
  - Outbreak responses
  - Door-to-door immunization campaigns
- Easy to deliver
  - Even children can give OPV doses
- Inexpensive

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

OPV: Disadvantages

- Poor immunogenicity in highest risk areas
- Interference between Sabin strains in tOPV
- Vaccine-associated paralytic poliomyelitis (VAPP): 250–500 cases/yr worldwide
  - Essentially uniform risk anywhere OPV used
  - OPV recipients: ~1 case/750,000 first OPV doses
  - Cases in unimmunized OPV contacts
- Risk of VDPV emergence

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

VDPVs

- Circulating VDPVs (cVDPVs)
  - Main risk factor: immunity gaps from low OPV coverage and absence of natural immunity
- Immunodeficiency-associated VDPVs (iVDPVs)
  - Primary B-cell (Ab) immunodeficiencies
  - T-cell immunodeficiencies (e.g., HIV-1 infection) apparently *not* a risk factor
  - iVDPVs rare even among immunodeficients
  - Effective therapies needed
- Ambiguous VDPVs (aVDPVs)
  - Provisional assignment; VDPV source unknown
  - Environmental isolates not linked to any patient
  - Isolates from patients with no known immunodeficiency
  - Single VDPV isolates (no known outbreak)

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

Shared Properties of VDPV Isolates

	iVDPVs	cVDPVs	aVDPVs
Associated with polio in humans	Usually[a]	Yes	Some[b]
Neurovirulent in Tg-CD155 mice	Yes[c]	Yes	Yes[c]
Loss of key attenuating substitutions	Yes	Yes	Yes
Replicate at 39.5 C	Yes	Yes	Yes
Antigenic divergence from Sabin parent	Yes	Yes[d]	Yes[d]

[a] Some iVDPVs isolated from immunodeficient carriers

[b] Some aVDPVs from the environment or healthy carriers

[c] When tested

[d] Antigenic divergence may not occur with all type 2 VDPVs

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

Distinguishing Properties of VDPV Isolates

	iVDPVs	cVDPVs	aVDPVs
Sabin/HEV-C recombination	No	Usually[a]	Some
Sabin/Sabin recombination	Some	Some[b]	Some
Isolates have diverse mixed populations	Some	No	Some
Person-to-person transmission	Rarely found[d]	Yes[c]	Rarely found[d]

[a] Includes all isolates from EGY, HAI-DOR, PHL, MAD, INO, MMR outbreaks and most from NIE outbreak

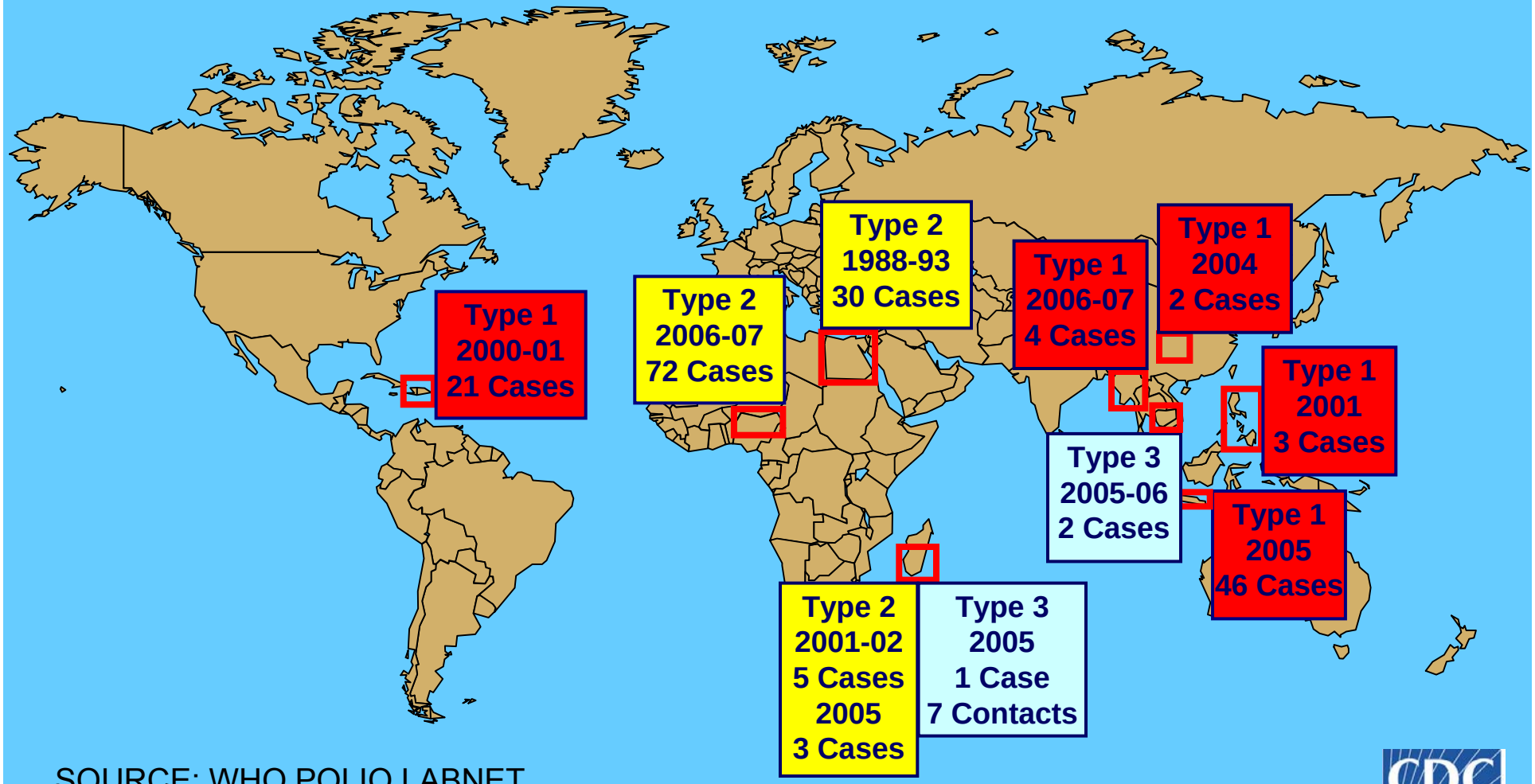
[b] cVDPV from LAO

[c] Closely related lineages found in cases and contacts

[d] Possible transmission in high-risk community and orphanage settings

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

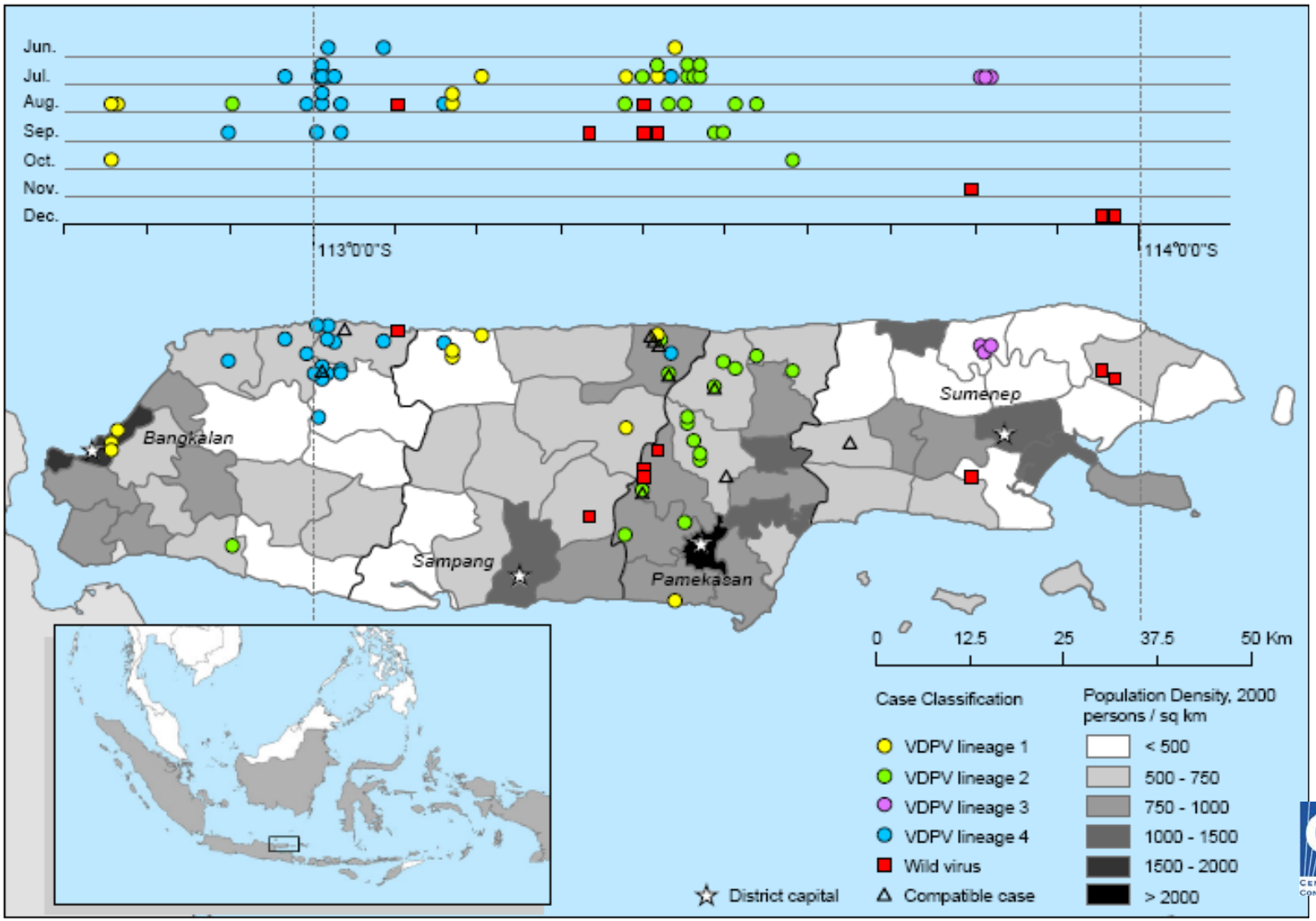
Circulating Vaccine-Derived Poliovirus Outbreaks, 1988–2007



SOURCE: WHO POLIO LABNET

CDC
Centers for Disease Control and Prevention

Geographic, Genetic and Temporal Distribution



Patient Characteristics: Madura cVDPV Outbreak

Case patients, no. (%)

	VDPV* (n=45)	WPV* (n=8)	Compatible* (n=10)
Male	21/45 (47%)	5/8 (63%)	5/10 (50%)
Age in years, median (range)	2 (0.5-14)	2.5 (1-10)	4 (1-8)
Children <5 years	36/45 (80%)	6/8 (75%)	6/10 (60%)
Fever	42/44 (95%)	8/8 (100%)	10/10 (100%)
Asymmetry	21/45 (46%)	1/8 (13%)	2/9 (22%)
Residual paralysis	29/45 (64%)	4/5 (80%)	7/9 (78%)
OPV <3 doses	37/41(90%)	6/7 (86%)	7/8 (88%)

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

NIE, NIG 05-07 PV2 cVDPV Outbreak - VP1 tree created 9 Sept 2007

Lineage 1

Lineage 2

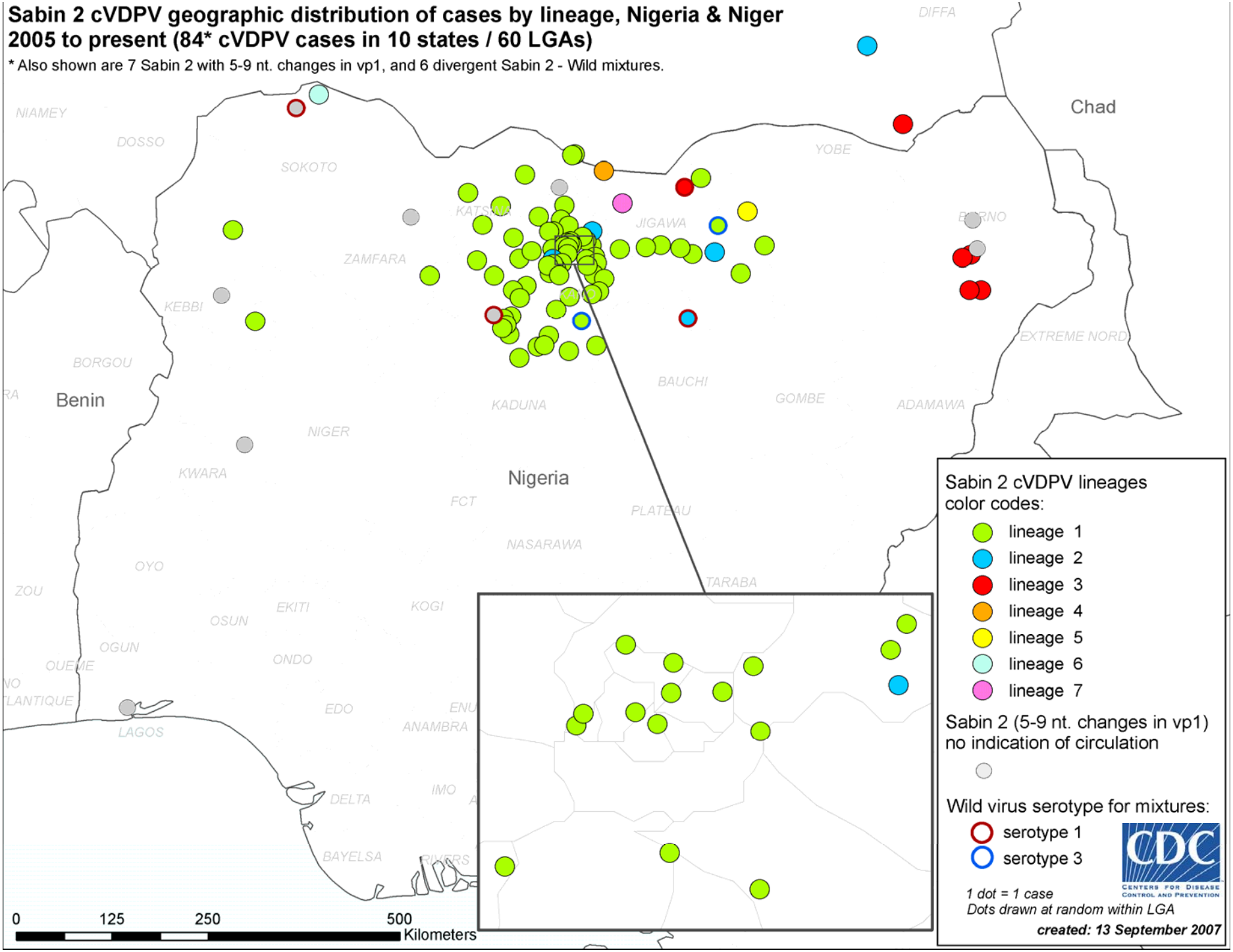
Lineage 3

Lineages 4-7

Tree colored by date of onset, red=2007, blue=2006 & black=2005

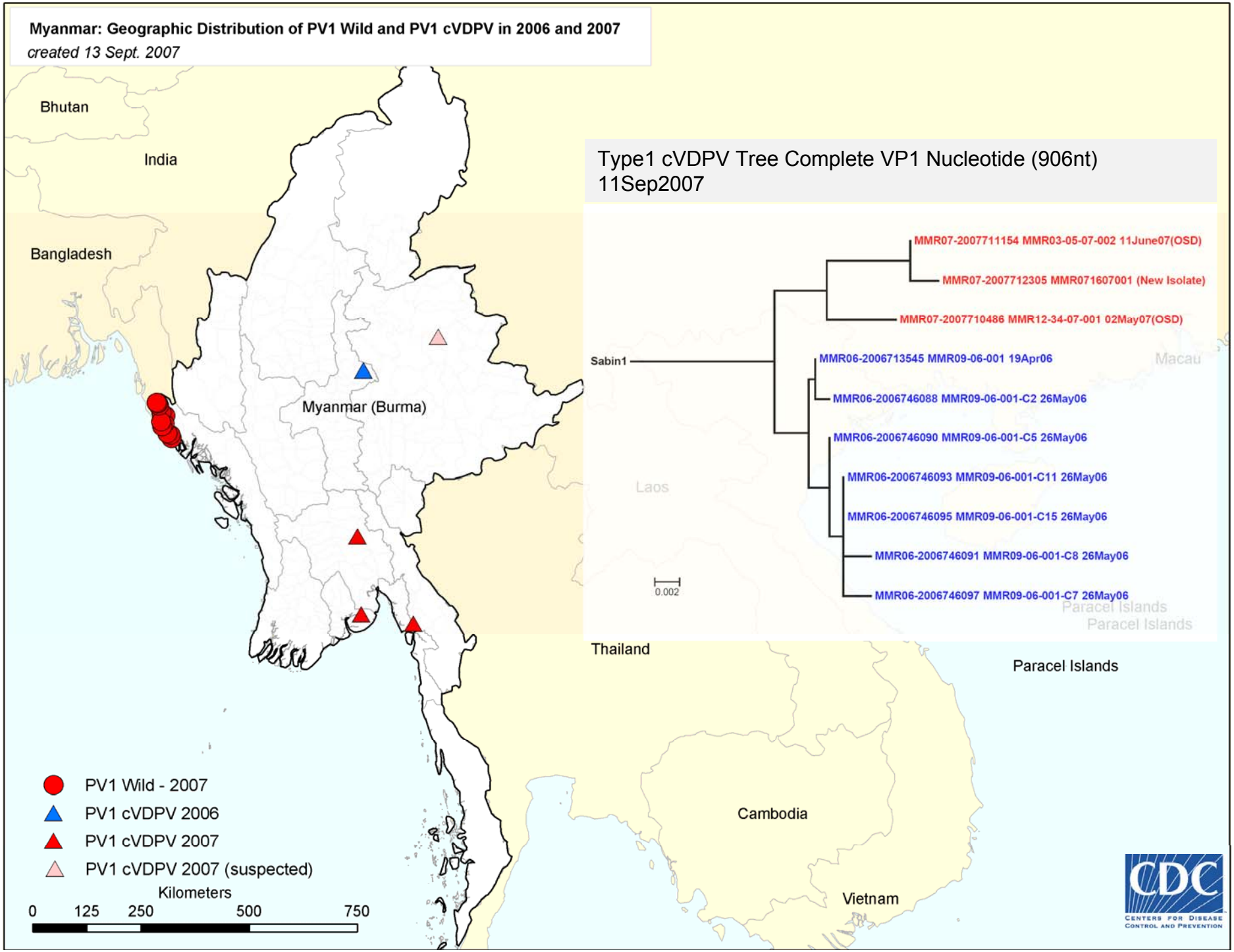
To be assigned a lineage the number of nt. In VP1 must be >= 10

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION


Sabin 2 cVDPV geographic distribution of cases by lineage, Nigeria & Niger
2005 to present (84* cVDPV cases in 10 states / 60 LGAs)
* Also shown are 7 Sabin 2 with 5-9 nt. changes in vp1, and 6 divergent Sabin 2 - Wild mixtures.
NIAMEY
DOSSO
SOKOTO
ZAMFARA
KEBBI
BORGOU
Benin
NIGER
KWARA
OYO
ZOU
OUEME
OGUN
LAGOS
EKITI
OSUN
ONDO
EDO
DELTA
BAYELSA
KOGI
ANAMBRA
IMO
KATSINA
JIGAWA
KADUNA
FCT
NASARAWA
PLATEAU
TARABA
BAUCHI
GOMBE
YOBE
DIFFA
Chad
BORNO
EXTREME NORD
ADAMAWA
Nigeria
0
125
250
500
Kilometers
Sabin 2 cVDPV lineages
color codes:
lineage 1
lineage 2
lineage 3
lineage 4
lineage 5
lineage 6
lineage 7
Sabin 2 (5-9 nt. changes in vp1)
no indication of circulation
Wild virus serotype for mixtures:
serotype 1
serotype 3
1 dot = 1 case
Dots drawn at random within LGA
created: 13 September 2007
CDC
Centers for Disease Control and Prevention

Myanmar: Geographic Distribution of PV1 Wild and PV1 cVDPV in 2006 and 2007

created 13 Sept. 2007



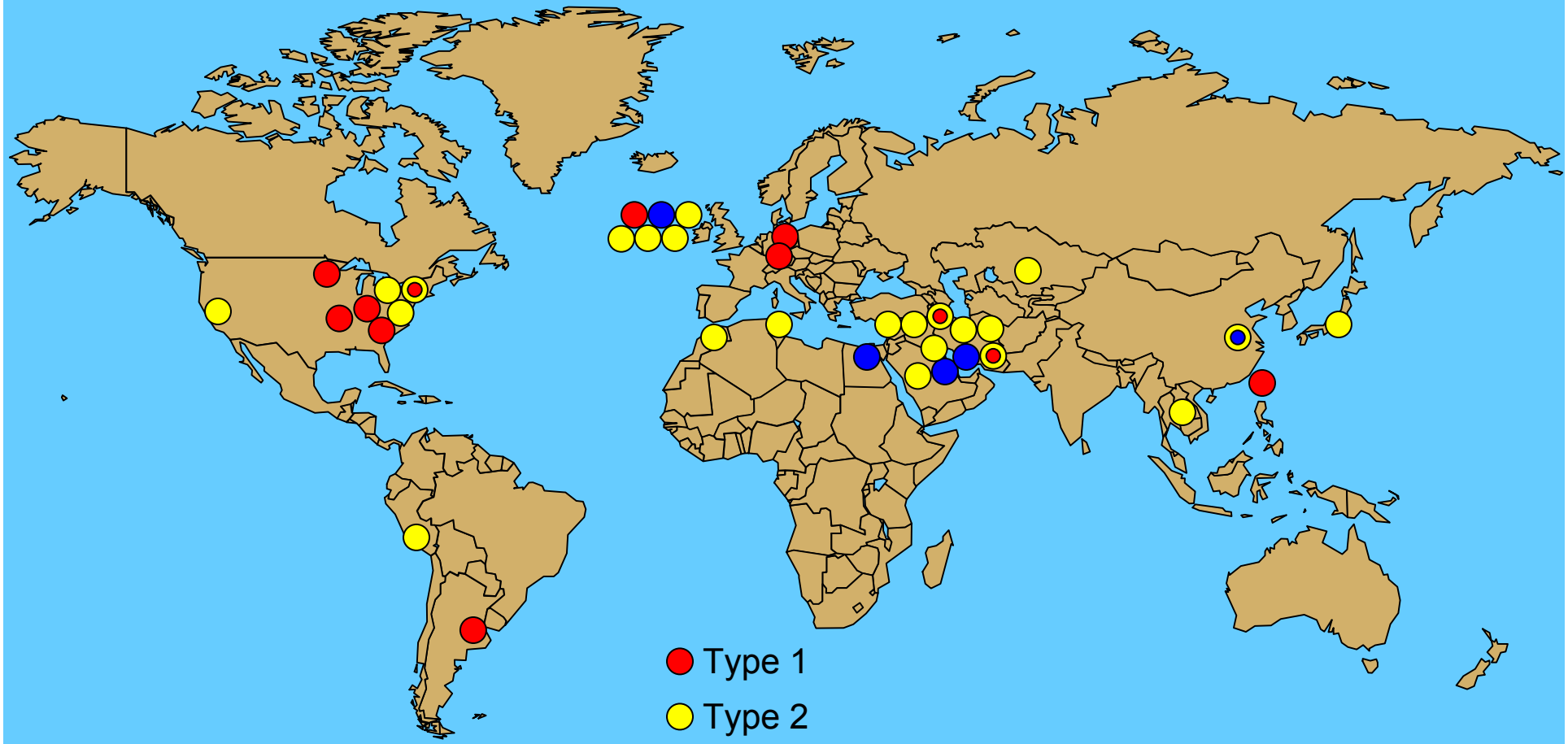
Type1 cVDPV Tree Complete VP1 Nucleotide (906nt)
11Sep2007

cVDPV "Lessons"

- cVDPVs can become endemic (Egypt, ~1983–93)
- cVDPVs of same serotype can repeatedly emerge (Madagascar, 2001–02; 2005)
- cVDPVs can emerge in isolated communities with low rates of vaccine coverage (Guizhou, CHN, 2004; Madura, INO, 2005–06; [Minnesota, USA, 2005])
- cVDPVs and wild polioviruses of the same serotype can co-circulate (Madura, INO, 2005–06)
- Multiple cVDPV lineages can independently emerge and co-circulate (Nigeria, 2005–07)
- Vaccine/HEV-C recombination not required for VDPV circulation (Guizhou, CHN, 2004; [Minnesota, USA, 2005])
- Traditional reservoir areas warrant special concern

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

Primary Immunodeficiency-Associated Vaccine-Derived Poliovirus Isolates, 1962–2007



SOURCE: WHO POLIO LABNET

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

Incomplete Data: longterm excretors

(iVDPVs: 1º immunodeficiency-associated VDPVs)

39 iVDPVs (> 6 mos excretion)

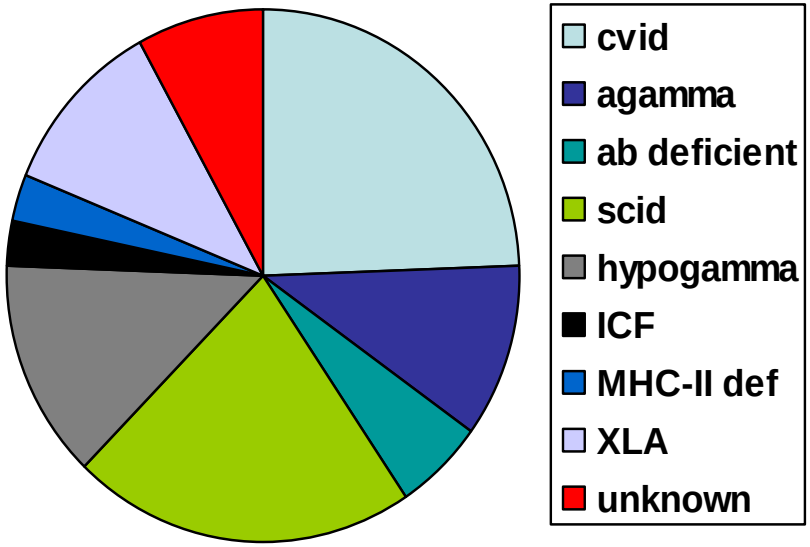
3 known to excrete >5 years.

Type 2 > Type 1 > Type 3

From:

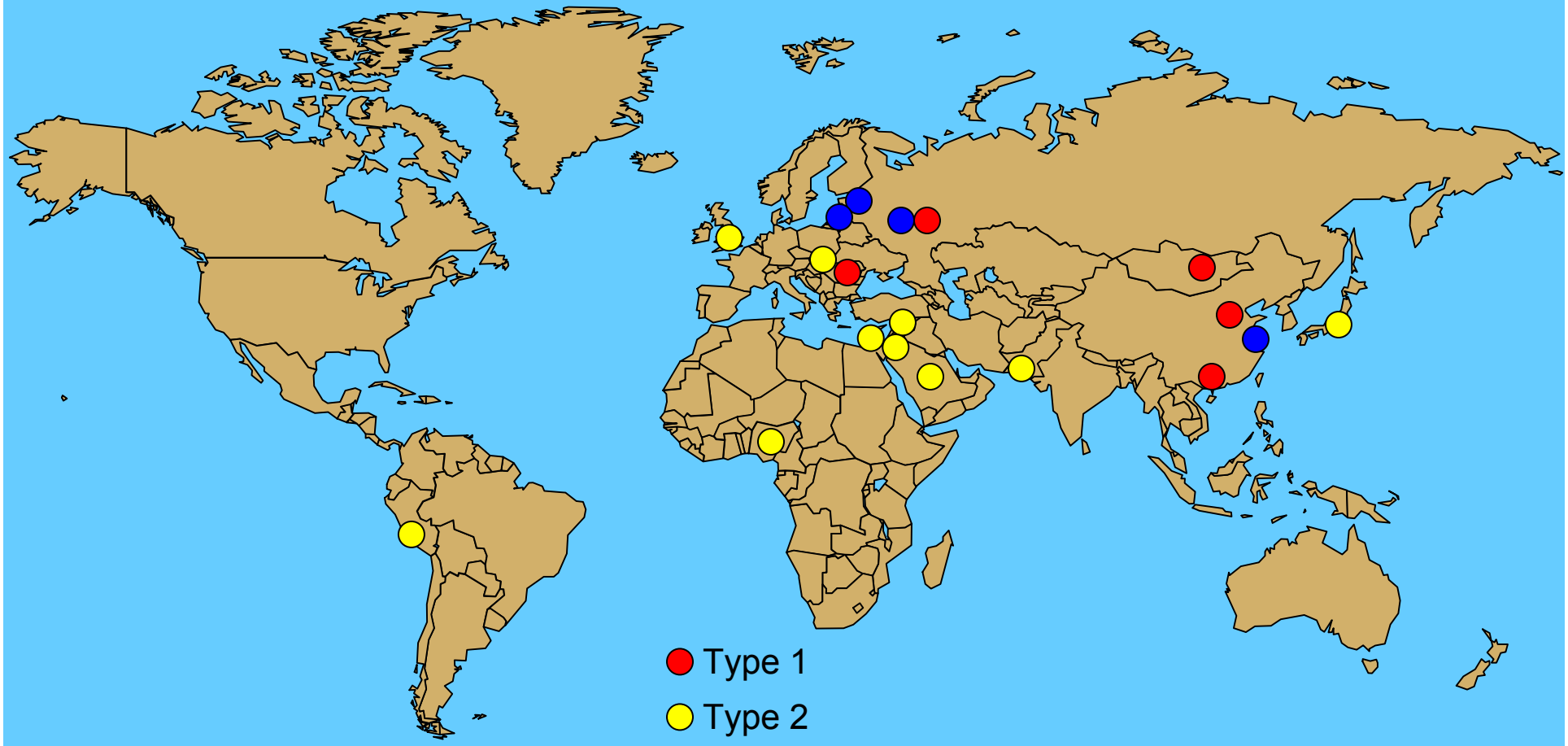
- High-income countries (22)
- Middle-income countries (15)
- Low-income countries (0)

Immunodeficiencies linked to prolonged poliovirus excretion



CDC
Centers for Disease Control and Prevention

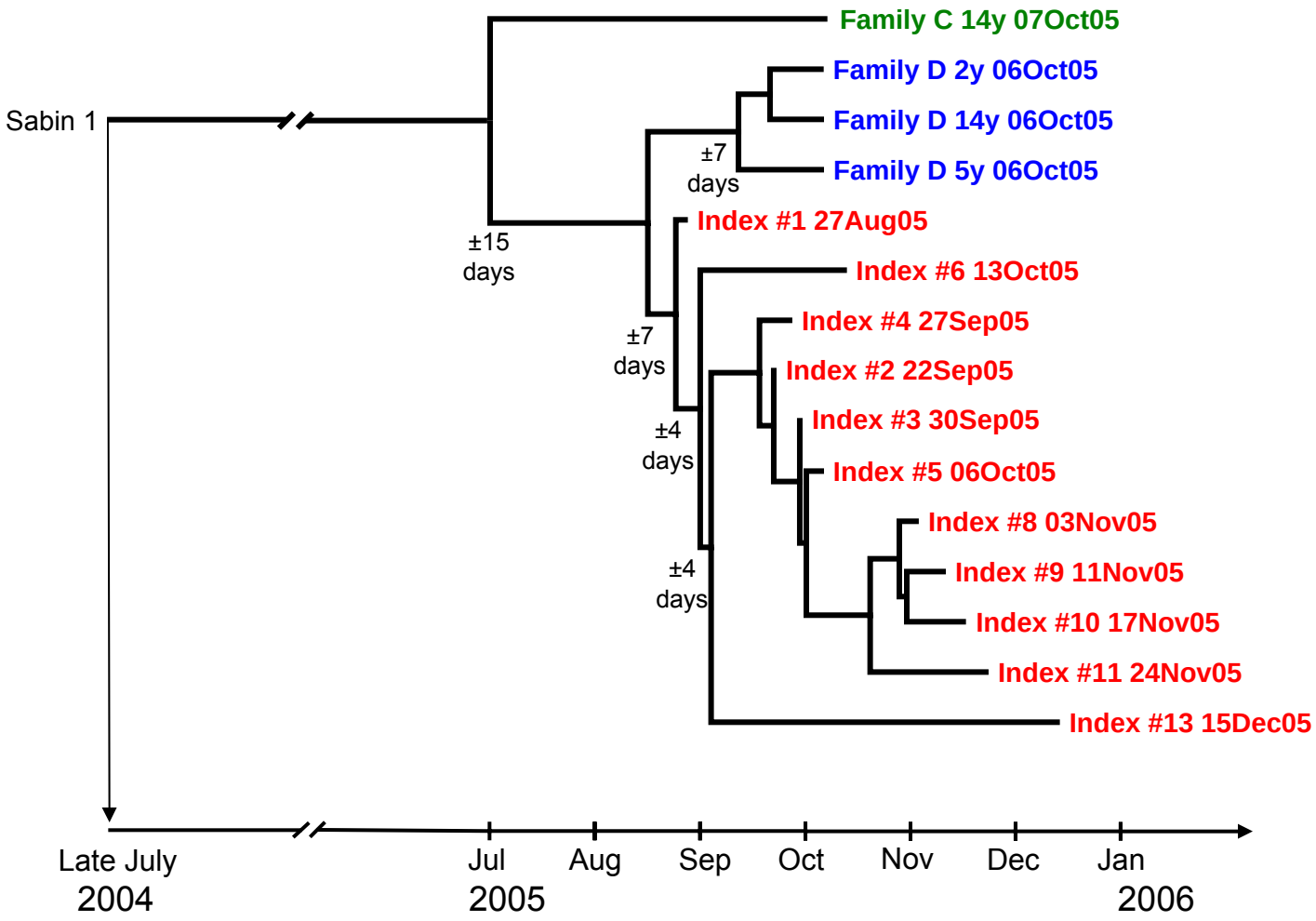
Ambiguous Vaccine-Derived Poliovirus Isolates, 1983–2007



SOURCE: WHO POLIO LABNET

CDC
Centers for Disease Control and Prevention

Minnesota/USA PV1/VDPVs: Estimated Timeline of Infections



Maximum Likelihood/TipDate: Complete Open Reading Frame Sequences

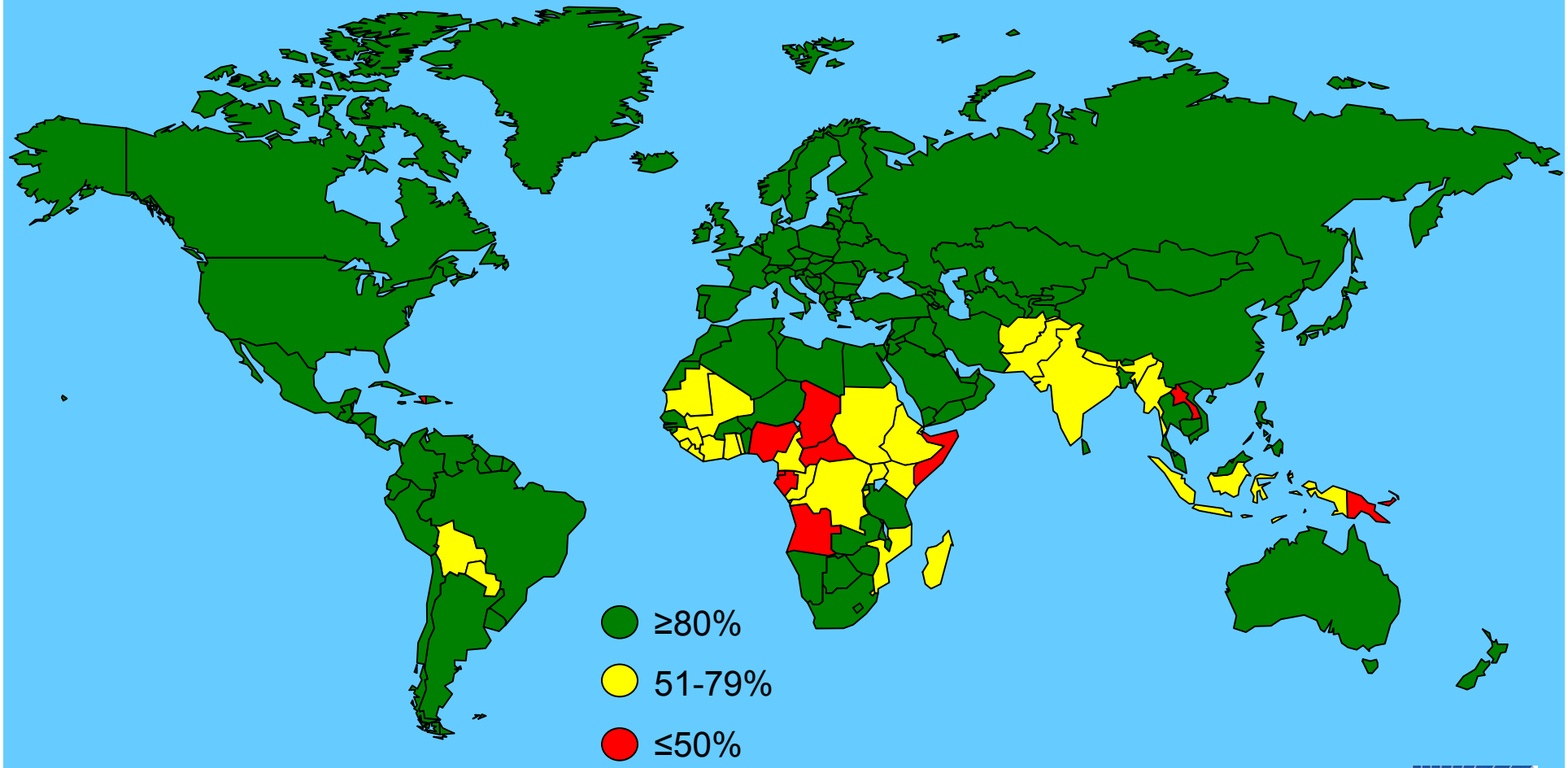
Global Surveillance for VDPVs

- WHO Global LabNet approach (since 2000)
  - Molecular characterization
    - PCR, real-time PCR, PCR-RFLP, or microarrays
  - Antigenic characterization
    - ITD-ELISA or neutralizing MAb
  - Discordant isolates → VP1 sequencing
  - From >20,000 vaccine-related isolates (1999--)
    - 10 independent cVDPVs (from the 10 recent outbreaks)
    - 29 independent iVDPVs
    - 18 independent aVDPVs
    - VDPVs <1% of all vaccine-related isolates

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

Routine OPV3 Coverage

UNICEF/WHO Estimates, 2005



SOURCE: UNICEF/WHO, 2006 Global Summary

CDC
Centers for Disease Control and Prevention

Summary

- OPV benefits currently outweigh risks in high-risk areas
- Risk profiles change with epidemiologic conditions
- VDPVs currently are rare
- High vaccine coverage prevents cVDPV emergence and spread
- iVDPVs are sporadic
  - New sensitive screening/detection methods in development
  - Effective therapies needed (new antivirals)
- Type 2 VDPVs are most frequent
- aVDPVs are probably uncategorized iVDPVs/cVDPVs
- VDPV risks are a critical component of endgame
- Routine vaccine coverage remains low in key countries

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION